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This month, *FASD in Review* examines a recent article by Lisbet Lundsberg, et al., in *Annals of Epidemiology*, titled "Low-to-Moderate Prenatal Alcohol Consumption and the Risk of Selected Birth Outcomes: a Prospective Cohort Study," Volume 25, 46-54, October 2014.

Overall Summary

Research on the relationship between birth outcomes and low to moderate levels of prenatal alcohol exposure often produces limited results based on a range of factors, including lack of controls for other variables, imprecise or variable measures of alcohol intake, subjective reporting bias (including recall problems and underreporting), and limited longitudinal study designs. While Lundsberg and colleagues utilize a design that addresses weaknesses in previous studies (e.g., strategies to minimize participant recall bias, data collection that is prospective and retrospective to birth outcomes, adjustments for numerous potential confounding variables), it lacks evidence on longer-term risk of alcohol use across the spectrum of disorders that have been documented as a result of alcohol use during pregnancy. Because media sources have reported inaccurately or incompletely about these research findings, public perception about risk of alcohol use during pregnancy may be influenced. However, there is no strong evidence to suggest any changes to the current public health policy on drinking during pregnancy — no amount of alcohol consumption can be considered safe.

Alcohol Consumption and Risk of Birth Outcomes - Background

In 2005, the U.S. Surgeon General released an advisory that established the current public health policy on alcohol use during pregnancy – no amount of alcohol consumption can be considered safe during those nine months. The advisory was issued based on the significant body of literature collected over the previous 30 years regarding the identification of Fetal Alcohol Spectrum Disorders (FASD) caused by prenatal alcohol exposure.

Ten years later, that public health policy remains intact, and research has led to increased specificity about the disorders within the overall spectrum, which include (Center for Substance Abuse Prevention, 2014):

- Fetal Alcohol Syndrome (FAS) individuals with abnormal facial features (facial dysmorphology), impaired growth, and cognitive and behavioral abnormalities;
- Partial Fetal Alcohol Syndrome (pFAS) individuals with FAS without growth deficiency, or FAS with most but not all of the facial features;
- Alcohol-Related Neurodevelopmental Disorder (ARND) individuals with prenatal alcohol exposure
 and neurodevelopmental abnormalities, but no FAS facial phenotype (Note: some diagnostic
 systems replace ARND with neurobehavioral disorder/alcohol exposed and static
 encephalopathy/alcohol-exposed see below);
- Neurobehavioral Disorder/Alcohol Exposed (ND/AE) prenatal alcohol exposure, moderate cognitive/behavioral impairment (equivalent to moderate ARND); and
- Static Encephalopathy/Alcohol-Exposed (SE/AE) individuals with prenatal alcohol exposure and severe cognitive/behavioral impairment, but no FAS facial phenotype (equivalent to severe ARND).

Alcohol-Related Birth Defects (ARBD) – individuals who present with congenital defects, but not
the growth or cognitive/ behavioral impairments typically seen in FAS. Now less used, although
diagnostic guidelines still exist through the Institute of Medicine (IOM).

Research continues to examine the specific interplay of factors that alter the impact of alcohol on a particular developing fetus, including dose of alcohol, pattern and timing of exposure, genetics, maternal use of other drugs and tobacco, general health and nutrition of the mother, stress and trauma during pregnancy, and age (Guerri, Bazinet, & Riley, 2009). The new study by Lundsberg and colleagues adds to the evidence base on alcohol use during pregnancy and immediate birth outcomes.

<u>Lisbet Lundsberg et al., "Low-to-Moderate Prenatal Alcohol Consumption and the Risk of Selected Birth Outcomes: a Prospective Cohort Study," Annals of Epidemiology, (25), 46-54, October 2014.</u>

This study examined the effects of low to moderate alcohol use during pregnancy on birth weight, preterm delivery, intrauterine growth restriction, and selected neonatal outcomes. The study population consisted of women who were enrolled in one of two study cohorts in Connecticut and Massachusetts; one a study on prenatal caffeine exposure and the other on asthma in pregnancy. The final study sample of 4,496 women was restricted to those women with live births. The cohorts included urban and suburban pregnant women from hospital clinics, community clinics, and private obstetrical offices.

Data were collected during two study visits, one baseline prenatal interview (completed before 24 weeks gestation) and one postpartum interview (typically in the hospital or within 1 month of delivery). Participants were asked about their alcohol use during months 1 to 3 of gestation during the baseline interview and about alcohol use for gestational month 7 and the third trimester at the postpartum interview. Second trimester alcohol use was not assessed. Gestational age was based on last menstrual period (LMP) or an ultrasound estimate if LMP was uncertain or inaccurate.

Women were asked about beverage type (wine, beer, and liquor), frequency of use, and number of drinks consumed per week for each of the time periods in question (first trimester, gestational month 7, and third trimester). A standard drink was defined as 0.5 ounces. The authors used a previously established algorithm (Jessor et al., 1968) to derive alcohol content values for each beverage that were then summed for a total exposure score expressed as daily ounces of alcohol for each month per trimester. Key outcomes of interest were defined as follows:

- Drinking levels* Six categories were used:
 - o 0 drinks;
 - o less than 1.5 drinks/week;
 - o 1.5 to less than 3.5 drinks/week;
 - 3.5 to less than 7 drinks/week;
 - o 7 to less than 14 drinks/week; and
 - o 14+ drinks/week.
- Low birth weight less than 2,500 grams
- Preterm delivery less than 37 weeks
- Intrauterine growth restriction less than 10th percentile of birth weight for gestational age according to 1999 U.S. birth standards, adjusted for gender and mother's ethnicity
- Low birth length and reduced head circumference lowest 10th percentile according to Centers for Disease Control and Prevention standards

*Note: It was unclear to the reviewer how the standard drink size was conveyed to the women, if differences were defined for each type of alcohol measured, and which categories were defined as low and moderate use. In addition, the algorithm used to derive alcohol content values was unable to be reviewed but was referenced as part of a study published in 1968 on society, personality, and deviant behavior in a small rural community.

Statistical analyses were performed to estimate the effects of early pregnancy drinking, month 7 drinking, and third trimester drinking on the birth outcomes specified above. Results suggested that low to moderate alcohol exposure during early and late gestation is not associated with increased risk of low birth weight, preterm delivery, intrauterine growth restriction, and most selected perinatal outcomes.

New or Notable Information

Study results included the following findings:

- Low to moderate alcohol consumption is not associated with an increased risk for specific birth outcomes and measures of fetal growth.
- Maternal alcohol exposure was most prevalent during the first month of pregnancy (29%); however, alcohol consumption was reported as curvilinear, becoming less frequent after recognition of pregnancy, and then modestly increasing through the third trimester.
- A strong relationship was found between caffeine and alcohol consumption in month 1 of pregnancy.
- Women who were smokers were more likely to be drinking during pregnancy than non-smokers.
- Women who exercised, worked, and took multivitamins were more likely to have consumed alcohol in month 1 of pregnancy.

Implications of the New Research

The key implications of this new research focus on alcohol risk and immediate birth outcomes among women who report low to moderate alcohol use during pregnancy. The key study limitations, and therefore the recommendations for future research on this topic, involve the needs for: 1) greater clarity on the alcohol consumption measurements; and 2) longitudinal follow-up to determine risk over time. The authors did not clearly define the actual use associated with low to moderate alcohol consumption, though they referenced the National Institute of Alcohol Abuse and Alcoholism web site for the definition of binge drinking (4 drinks for women and 5 drinks for men in a 2-hour period). The same web site uses the Dietary Guidelines for Americans to define moderate drinking (up to 1 drink per day for women and up to 2 drinks per day for men), but there was no explicit reference to the use of this definition in the current study. In addition, a standard drink is typically defined differently for wine, beer, and alcohol, although the study authors appear to have utilized a single measurement of 0.5 ounces across all alcohol types. It was also unclear how the women were asked about this measurement (i.e., verbal description only, verbal description with pictures, etc.), an important detail as this is a variable that is often underestimated in self-reports (Muggli et al., 2014; Henderson, Gray, & Brocklehurst, 2007). Finally, the algorithm utilized is based on a study that is over 40 years old, raising questions about consistencies with current standards used to measure alcohol content values.

The current study contributes to other findings that provide a lack of support for increased risk for specified birth outcomes based on low to moderate alcohol exposure (Bakker et al., 2010; Polygenis et al., 1998; Walpole, Zubrick, & Pontre, 1990; Shiono, Klebanoff, & Rhoads, 1986). However, this and other studies assessing alcohol risk on immediate birth outcomes fall short of contributing new evidence about *long-term* risk of alcohol use during pregnancy on offspring, as this relationship requires

longitudinal follow-up to assess growth and cognitive, behavioral, and neurological functioning over time.

Misperceptions about these study findings are being observed in current media. While Lundsberg and colleagues acknowledge some of the limitations addressed above in an interview for the Yale School of Public Health in November 2014, media on the findings is mixed in terms of reporting the full story. For example, in one recent article summarizing the findings, the title was "Small Alcohol Consumption in Pregnancy Won't Hurt Baby" (Nature World News, November 24, 2014). While the actual article provides balanced reporting of the study, the title has the unintended yet potentially significant and costly consequence of misinforming the public about the potential risk involved with alcohol use during pregnancy – even at low to moderate levels. This is especially concerning, as the title could easily be conveyed through Twitter and other social media tools as carrying the weight of public policy. (To help raise accurate awareness and prevent alcohol use during pregnancy, join the conversation by using #Odrinks9months.)

Ultimately, the current study is a useful addition to the body of literature on alcohol and pregnancy, and offers an opportunity for follow-up research that could help to better define the risk of short-term and long-term alcohol use. However, there is no strong evidence to suggest any change to the Surgeon General's policy on drinking during pregnancy – no amount of alcohol consumption can be considered safe.

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